

## **REMARKS**

### **1. Amendments to the Specification**

The specification has been amended to correct inadvertent typographical errors. Support for these amendments can be found throughout the application, for example, in Example 3. Thus, these amendments introduce no new matter.

### **2. Status of the Claims and Support for the Amendments to the Claims**

Claims 1-9 and 18-23 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue and claim the subject matter of these canceled claims in one or more divisional or continuation patent applications.

Claims 10-17 and 24 have been amended and new claims 25-29 have been added. Support for the amendments and for the new claims can be found throughout the specification. For example, support for the amendments to claim 1 can be found in the specification at page 3, lines 23-31; at page 4, lines 16-20; and throughout pages 6-7. The amendments to claims 11-17 and 24 are sought bring the claims into conformance with U.S. practice and to more clearly present Applicants' invention. Support for new claims 25-29 can be found, for example, in Example 3 at pages 15-17. The foregoing amendments do not add new matter, and entry and consideration are respectfully requested.

Upon entry of the foregoing amendments, claims 10-17 and 24-29 are pending in the application, with claims 10 and 25 being the independent claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

### **3. The Objections to the Specification Should be Withdrawn**

In the Office Action at page 2, paragraphs 5-7, the specification has been objected to for various informalities. Specifically, the Office Action indicates that the specification contains instances of the the term "silicon oil," which appears to be a misspelling of "silicone oil," and that untranslated German preposition "von" appears at page 26. In addition, the Office Action notes that the claims are not the object of a sentence.

Applicants appreciate the Office Action pointing out these inadvertent errors. By the foregoing amendments to the specification, these errors have been corrected. Thus, Applicants respectfully request withdrawal and reconsideration of the objections to the specification.

**4. The Rejection of Claims 1-7, 9-16 and 18 Should be Withdrawn**

In the Office Action at pages 3-7, paragraphs 8-28, claims 1-7, 9-16 and 18 have been rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Bloch *et al.*, U.S. Patent No. 5,411,876 (hereinafter “Bloch”), as evidenced by Wolfmeier *et al.*, “Waxes” in *Ullmann's Encyclopedia of Industrial Chemistry* (2000) (hereinafter “Wolfmeier”). Claims 1-9 and 18 have been canceled without prejudice or disclaimer. Hence, this rejection has been rendered moot as it may have applied to these claims. Applicants respectfully traverse this rejection as it may apply to the remaining claims.

The Office Action contends that Bloch discloses a contamination barrier comprising a layer of grease, wax or mineral oil, used to seal an aqueous solution in a PCR tube. The Office Action asserts, as allegedly evidenced by Wolfmeier, that waxes are composed of hydrocarbon mixtures. The Office Action also asserts that Bloch discloses that the waxes can be comprised of substituted or unsubstituted hydrocarbons of various lengths, as well as saturated or unsaturated cyclic hydrocarbons, or branched or unbranched acyclic hydrocarbons.

The Office Action also asserts that Bloch discloses a method for preventing contamination during processing of an aqueous solution, as the use of wax to cover the aqueous solutions in PCR wells acts as a vapor barrier that also prevents contamination. The Office Action therefore concludes that the claimed invention is anticipated. Applicants respectfully disagree with these contentions and conclusions.

Present claim 10 (and hence, claims 11-16 that depend ultimately therefrom) recites a method for preventing contamination during the processing of aqueous solutions in open and automated systems comprising covering the aqueous solutions with a contamination barrier comprising at least one water immiscible hydrocarbon or hydrocarbon mixture. The covering prevents contamination during transfer of the aqueous solutions, and/or the covering prevents formation of aqueous aerosols, while still allowing for removal and processing of the aqueous solutions under the contamination barrier. The at least one water immiscible hydrocarbon or hydrocarbon mixture comprises branched or unbranched hydrocarbons of from 6 to 16 carbon atoms.

Applicants respectfully submit that Bloch does not disclose a method for preventing contamination during the processing of aqueous solutions in open and automated systems comprising covering the aqueous solutions with a contamination barrier comprising at least one water immiscible hydrocarbon or hydrocarbon mixture, wherein the at least one water immiscible hydrocarbon or hydrocarbon mixture comprises branched or unbranched hydrocarbons of from 6 to 16 carbon atoms. Applicants note that compositions disclosed in Bloch are limited to waxes comprising at least 20

carbons. See Bloch at column 11, lines 25-28. In fact, the Office Action concedes that Bloch does not disclose “that the contamination barrier is selected from the group consisting of octane, nonane, decane and dodecane and mixtures thereof.” Office Action at page 8, paragraph 33. In addition, claims 19-24 were not rejected in the Office Action under 35 U.S.C. § 102(b), over Bloch, further evidencing that the Office Action did not consider these claims potentially anticipated by Bloch.

Applicants respectfully submit that as Bloch does not disclose each and every element of the presently claimed invention, Bloch cannot and does not anticipate the present claims. See M.P.E.P. § 2132. In view of the foregoing remarks, reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) are respectfully requested.

**5. The Rejection of Claims 8, 17 and 19-24 Under 35 U.S.C. § 103(a) Over Bloch in View of Perbost Should be Withdrawn**

In the Office Action at pages 8-10, paragraphs 29-39, claims 8, 17 and 19-24, have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Bloch in view of Perbost *et al.*, U.S. Published U.S. Patent Application No. 2002/0086327 (hereinafter “Perbost”). Claims 19-23 have been canceled. Hence, this rejection has been rendered moot as it may have applied to these claims. Applicants respectfully traverse this rejection as it may apply to the remaining claims.

The Office Action asserts that Bloch allegedly discloses Applicants’ invention as set forth above. However, the Office Action concedes that Bloch does not explicitly disclose that the contamination barrier is selected from the group consisting of octane, nonane, decane and dodecane and mixtures thereof. See Office Action at page 8, paragraph 33. The Office Action attempts to cure this deficiency with the disclosure of Perbost.

Specifically, the Office Action asserts that Perbost discloses a method of shielding biosynthesis arrays from the surrounding environment by applying a non-miscible fluid to the array. The Office Action indicates that Perbost discloses that the non-miscible fluids can comprise hydrocarbons selected from the group consisting of octane, nonane, decane and dodecane and mixtures thereof. The Office Action contends that it would have been obvious to modify the contamination barrier allegedly disclosed in Bloch to include the non-miscible fluid shields of Perbost in order to provide an inert and insoluble barrier. The Office Action therefore concludes that the claimed invention would have been obvious. Applicants respectfully disagree with the contentions and conclusions in the Office Action.

Applicants submit that the obviousness rejection set forth in the Office Action is based on impermissible hindsight. See M.P.E.P. § 2145.X.A; *see also KSR Int'l. Co. v. Teleflex Inc.*, 127 S.Ct.

1727, 1752 (2007). (“A factfinder should be aware, or course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning.”) The Office Action has not set forth a proper *prima facie* case of obviousness. As set forth in M.P.E.P. § 2143(D), a *prima facie* case of obviousness can only be shown where the cited combination of references would yield predictable results. *See KSR*, 127 S.Ct. 1727 at 1740. The Office Action has not provided a showing that modifying the disclosure of Bloch with the disclosure of Perbost would have a reasonable expectation of success --- i.e., a reasonable expectation that modifying the greases and waxes utilized in Bloch, as required, would result in a successful method of preventing contamination. Absent such a showing, a *prima facie* case of obviousness cannot be established. *See* M.P.E.P. § 2143.02. In addition, Applicants submit that the modification proposed in the Office Action is impermissible, as it would render the primary reference of Block unsatisfactory for its intended purpose. *See* M.P.E.P. § 2143.01.V.

**5.1 Bloch and Perbost would not have provided a reasonable expectation for successfully preventing contamination**

Applicants submit that the disclosure of Bloch relies on the use of greases or waxes to create a overlay on the surface of a PCR product. *See* Bloch at columns 3-4. The Office Action suggests that it would have been obvious to substitute the hydrocarbons octane, nonane, decane and dodecane, allegedly disclosed in Perbost, for the long chain hydrocarbon waxes disclosed in Bloch. Applicants submit that the Office Action has provided no indication that such a substitution would result in a barrier that would prevent contamination of an aqueous solution, as recited in the presently claimed invention. The fact that Perbost utilizes such hydrocarbons to provide a shield for biochemical reactions does not mean that such materials can be utilized for preventing contamination during the processing of aqueous solutions in open and automated systems, as recited in the presently claimed invention. Such a modification would not yield predictable results, and thus, cannot support a *prima facie* case of obviousness. *See* M.P.E.P. § 2143.02. *See also KSR*, 127 S.Ct. at 1740.

**5.2 The modification of Bloch by Perbost would render Bloch unsatisfactory for its intended purpose**

The methods disclosed in Bloch require a barrier that can transition from a solid at room temperature, to a liquid during PCR cycling.

The present invention provides an especially effective mode of reagent segregation by providing means to replace the mineral oil overlay with a layer of grease or wax, *the solidity of which at room temperature or below* creates a barrier against mixing of

aqueous reagents segregated above and below the grease or wax layer. *Thermal cycling [turns] the solid barrier into a lighter-than-water liquid*, which is displaced by an aqueous layer above; the upper aqueous layer contains all PCR reagents not present in the lower aqueous layer. Consequently, reagents previously segregated mix to create a complete reaction with the help of the considerable thermal convection which accompanies heating of the reaction tube. The melted grease or wax creates a vapor barrier to minimize solvent evaporation during thermal cycling and, upon cooling after amplification is complete, re-forms a solid barrier which, among other things, reduces the ease of PCR product dispersal into the environment when reaction tubes are opened, thereby reducing the likelihood of back-contaminating later reactions.

Bloch at column 4, lines 33-53 (emphasis added). Applicants submit that substituting a hydrocarbon consisting of octane, nonane, decane and dodecane, as disclosed in Perbost, for the greases and waxes disclosed in Bloch, would render Bloch unsatisfactory for its intended purpose.

As set forth in the attached Exhibit A (Table 2.1 in Organic Chemistry, Third Edition, Louden, G.M., Ed.), the melting points of octane, nonane, decane and dodecane are all below 0°C. Thus, at room temperature (approximately 23-25°C), these hydrocarbons would exist as a *liquid*, not a *solid*. If such hydrocarbons were utilized as barriers in the methods of Bloch, as suggested in the Office Action, it would not be possible for such barriers to exist as a solid at room temperature, and turn into a lighter-than-water liquid, with the thermal cycling utilized in PCR. Thus, the modification proposed in the Office Action would render the primary reference of Bloch unsatisfactory for its intended purpose -- the formation of a layer that cycles between solid and liquid during PCR thermal cycling. As set forth in Bloch:

The melted grease or wax creates a vapor barrier to minimize solvent evaporation during thermal cycling and, *upon cooling after amplification is complete, re-forms a solid barrier* which, among other things, reduces the ease of PCR product dispersal into the environment when reaction tubes are opened, thereby reducing the likelihood of back-contaminating later reactions.

Bloch at column 4, lines 46-53 (emphasis added).

Applicants submit that such a modification to Bloch is not permissible in the manner suggested in the Office Action. See M.P.E.P. § 2143.01.V. (If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. See *In re Gordon*, 733 F.2d 900 (Fed. Cir. 1984)). Thus, Applicant submits that the Office Action has not set forth a *prima facie* case of obviousness. See M.P.E.P. § 2143.

**5.3 The modification of Bloch by Perbost would change the principle of operation of Bloch**

As noted above, Bloch utilizes a barrier that transitions from a solid at room temperature to a liquid under PCR cycling:

The present invention provides an especially effective mode of reagent segregation by providing means to replace the mineral oil overlay with a layer of grease or wax, *the solidity of which at room temperature or below* creates a barrier against mixing of aqueous reagents segregated above and below the grease or wax layer. *Thermal cycling [turns] the solid barrier into a lighter-than-water liquid*, which is displaced by an aqueous layer above; the upper aqueous layer contains all PCR reagents not present in the lower aqueous layer.

Bloch at column 4, lines 33-53 (emphasis added). Applicants submit that substituting a hydrocarbon consisting of octane, nonane, decane and dodecane, as disclosed in Perbost, for the greases and waxes disclosed in Bloch, would change the principle of operation of Bloch.

As discussed above, octane, nonane, decane and dodecane would be *liquids, not solids* at room temperature. If such hydrocarbons were utilized as barriers in the methods of Bloch, as suggested in the Office Action, it would not be possible for such barriers to exist as a solid at room temperature, and turn into a lighter-than-water liquid, with the thermal cycling utilized in PCR. Thus, the modification proposed in the Office Action would change the principle of operation of Bloch -- thermal cycling of a layer between solid and liquid during PCR.

Applicants submit that such a modification to Bloch is not permissible in the manner suggested in the Office Action. *See* M.P.E.P. § 2143.01.VI. (If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *See In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)). Thus, Applicant submits that the Office Action has not set forth a *prima facie* case of obviousness. *See* M.P.E.P. § 2143.

In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

**CONCLUSION**

Applicant believes that the claims are in condition for allowance and respectfully request allowance thereof. The Examiner is invited to telephone the undersigned if that would be helpful in resolving any issues.

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 50-5071.

Respectfully submitted,

Date: April 13, 2010

By: /Jeffrey K. Mills/

Jeffrey K. Mills  
Registration No.: 56,413  
Attorney for Applicants

**Fanelli Strain & Haag PLLC**  
**Customer No. 91436**  
1455 Pennsylvania Ave N.W., Suite 400  
Washington, D.C., 20004  
Tel: 202.621.1840  
Fax: 202.621.1844